

Attorney Docket No.: 23546-08263

Client Ref.: ISIS-2960

Application No.: 09/067,638

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

83. (Currently amended) A system of associated components for preparing a set of oligonucleotides that ~~possess at least one property~~ modulates expression of a selected nucleic acid comprising:

a computer ~~network~~ system that prepares a virtual library of oligonucleotides targeted to ~~[[a]] said~~ selected nucleic acid and generates synthesis instructions in computer manipulable form for each of said oligonucleotides in said virtual library, wherein said computer ~~network~~ system reduces the members of said virtual library of oligonucleotides by a process of selection based on targeting a functional region of said selected nucleic acid;

an automated synthesizer that receives said synthesis instructions from said computer ~~network-system~~ and synthesizes a set of real oligonucleotides corresponding to said virtual set of oligonucleotides having reduced members; and

an apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular members of said set ~~possessing said at least one property that modulate expression of said~~ selected nucleic acid, wherein said procedure is computer-controlled polymerase chain reaction or computer-controlled enzyme-linked immunosorbent assay.

84. (Currently amended) The system of claim 83 wherein said functional region is the transcription start site, 5' cap, start codon, 5' UTR untranslated region, 3' UTR untranslated region, stop codon, 5' splice site or polyadenylation site.

85. (Currently amended) A system of associated components for preparing a set of oligonucleotides that ~~possess at least one property~~ modulates expression of a selected nucleic acid comprising:

a computer ~~network~~ system that prepares a virtual library of oligonucleotides targeted to ~~[[a]] said~~ selected nucleic acid and generates synthesis instructions in computer manipulable form for each of said oligonucleotides in said virtual library, wherein said computer ~~network~~ system reduces the members of said virtual library of oligonucleotides by one or more of i) a process of selection based on target accessibility to said selected nucleic acid, ii) a process of selection based on uniform distribution of oligonucleotide compounds across said selected nucleic acid, or iii) a process of selection based on targeting a functional region of said selected nucleic acid;

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an automated synthesizer that receives said synthesis instructions from said computer network system and synthesizes a set of real oligonucleotides corresponding to said virtual set of oligonucleotides having reduced members;

a first apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular members of said set ~~possessing said at least one property~~ that modulate expression of said selected nucleic acid, wherein said procedure is computer-controlled polymerase chain reaction or computer-controlled enzyme-linked immunosorbent assay; and

a second apparatus selected from the group consisting of liquid chromatography, optical density reader, mass spectroscopy, gel fluorescence and scintillation imaging, and capillary gel electrophoresis.

86. (Currently amended) A system of associated components for preparing a set of oligonucleotides that ~~possess at least one property~~ modulates expression of a selected nucleic acid comprising:

a computer network system that prepares a virtual library of oligonucleotides targeted to ~~[[a]]~~ said selected nucleic acid and generates synthesis instructions in computer manipulable form for each of said oligonucleotides in said virtual library, wherein said computer network system reduces the members of said virtual library of oligonucleotides by one or more of i) a process of selection based on target accessibility to said selected nucleic acid, ii) a process of selection based on uniform distribution of oligonucleotide compounds across said selected nucleic acid, or iii) a process of selection based on targeting a functional region of said selected nucleic acid;

an automated synthesizer that receives said synthesis instructions from said computer network system and synthesizes a set of real oligonucleotides corresponding to said virtual set of oligonucleotides having reduced members; and

an apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular members of said set ~~possessing said at least one property~~ that modulate expression of said selected nucleic acid, wherein said procedure is computer-controlled polymerase chain reaction or computer-controlled enzyme-linked immunosorbent assay, and wherein said property is modulating said selected nucleic acid.

87. (Currently amended) A system of associated components for preparing a set of oligonucleotides that ~~possess at least one property~~ modulates expression of a selected nucleic acid comprising:

a computer network system that prepares a virtual library of oligonucleotides targeted to ~~[[a]]~~ said selected nucleic acid and generates synthesis instructions in computer manipulable form for each of said oligonucleotides in said virtual library, wherein said computer network system reduces the members of said virtual library of oligonucleotides by one or more of i) a process of selection based on target accessibility to said selected nucleic acid, ii) a process of

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selection based on uniform distribution of oligonucleotide compounds across said selected nucleic acid, or iii) a process of selection based on targeting a functional region of said selected nucleic acid; wherein said computer ~~network~~ system searches at least one database for alternative transcripts;

an automated synthesizer that receives said synthesis instructions from said computer ~~network~~ system and synthesizes a set of real oligonucleotides corresponding to said virtual set of oligonucleotides having reduced members; and

an apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular members of said set ~~possessing said at least one property~~ that modulate expression of said selected nucleic acid, wherein said procedure is computer-controlled polymerase chain reaction or computer-controlled enzyme-linked immunosorbent assay.